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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,307	01/07/2002	Stephen Kent	229752001400	2826

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,307	KENT ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06172004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the response filed 16 June, 2004, wherein claims 36 and 37 were canceled without prejudice or disclaimer. No claim amendments accompanied the response. Claims 1-35 and 38 are currently under examination.

37 C.F.R. § 1.98

The information disclosure statement filed 17 June, 2004, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were

made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-8, 17-20, and 38 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Paoletti *et al.* (1998) in view of Ramshaw *et al.* (1999). As previously set forth, Paoletti and colleagues provide avipox viral vectors (e.g., TROVAC, ALVAC) encoding lentiviral (e.g., HIV, SIV) gene products (e.g., Gag, Pol, Env) that are suitable for inducing viral-specific immune responses. This teaching does not disclose the utilization a second nucleic acid encoding a cytokine that functions as an adjuvant. However, Ramshaw and colleagues provide recombinant viral vectors carrying a first nucleic acid encoding a viral immunogen (e.g., HIV-1) and a second nucleic acid encoding a cytokine adjuvant (e.g., IL-2, γ-IFN) that facilitates the immune response to the immunogen. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to modify the expression vectors of Paoletti *et al.* (1998), to include a second nucleic acid encoding a cytokine adjuvant as taught by Ramshaw *et al.* (1999), since this would reasonably be expected to enhance the immune response to the HIV-1 antigen of interest. Both the motivation and a reasonable expectation of success were clearly present in the prior art.

Applicants traverse and submit that there is no motivation to arrive at the claimed invention. This position is clearly untenable in view of the prior art. There is no question that Ramshaw *et al.* (1999) teach that the inclusion of a nucleotide sequence encoding a cytokine (e.g., IL-2, γ-IFN), as well as, a nucleotide sequence encoding a heterologous antigen (e.g., HA), in the genetic

background of a poxvirus (e.g., vaccinia virus) results in strong immune response against the heterologous antigen. The only limitations of this teaching is that it does not disclose an avipox virus construct or a heterologous HIV antigen. Paoletti and colleagues provide avipox viral vectors (e.g., TROVAC, ALVAC) encoding lentiviral (e.g., HIV, SIV) gene products (e.g., Gag, Pol, Env) that are suitable for inducing viral-specific immune responses. Thus, there would have been more than sufficient motivation to modify the compositions of Paoletti *et al.* (1998), to include a second nucleic acid encoding a cytokine adjuvant as taught by Ramshaw *et al.* (1999), since this would reasonably be expected to enhance the immune response to the HIV-1 antigen of interest. Contrary to applicants' assertion, both the motivation and a reasonable expectation of success were clearly present in the prior art.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-16 and 21-35 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are all directed toward HIV vaccine compositions, methods of making said compositions, and attendant methods of use to prevent HIV transmission or provide a therapeutic response in HIV-infected

individuals. The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). As previously set forth, the courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The state-of-the-art relative to HIV vaccine development is replete with failure. The development of an efficacious HIV vaccine has proven to be arduous. There are a number of factors that have precluded the successful development of an HIV vaccine including some of the following: (I) a lack of understanding of the correlates of protective immunity; (ii) a lack of understanding of protective immunogens, suitable adjuvants, routes of administration, and immunization regimens; (iii) the quasispecies nature of HIV replication leads to immune escape and effete immune responses; and (iv) the lack of an adequate animal model in which to assess vaccine efficacy (Haynes *et al.*, 1996; Lee, 1997; Letvin, 1998; Burton and Moore, 1998; Johnston, 2000; Feinberg and Moore, 2002).

2) The disclosure fails to provide adequate guidance pertaining to the correlates of protective immunity. In order to assess the effectiveness of any given putative vaccine, the skilled artisan needs to know the specificity and titer of those immune responses

that induce protection or provide some sort of therapeutic effect. However, to date these correlates are not known and the disclosure fails to provide any further illumination on the subject. Thus, the skilled artisan cannot reasonably ascertain if any given putative vaccine composition will be protective.

3) The disclosure fails to provide adequate guidance pertaining to suitable immunogens, adjuvants, routes of administration, and immunization regiments. Since the correlates of protective immunity remain to be elucidated, the skilled artisan cannot begin to predict which form the immunogen of interest should take (i.e., whole inactivated virus; live attenuated virus; subunit immunogen; combination of multiple immunogens in various forms), the appropriate adjuvants to be included, suitable routes of administration, or suitable immunization regimens. The disclosure fails to provide any further illumination on the subject.

4) The disclosure fails to provide any working embodiments. While it was noted that the specification described challenge studies involving one of the claimed compositions and a macaque model, many of the parameters of this study were not clearly disclosed (i.e., challenge virus, inoculating dose, etc.). In any event, the macaque model is clearly not predictive of clinical efficacy due to the various genotypic and phenotypic differences between macaques, humans, and the lentiviruses that infect them. Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Applicants traverse and submit that the disclosure fully supports the breadth of the claimed invention. This position is clearly untenable in view of the state-of-the-art vis-à-vis HIV vaccine development. The crux of the rejection is not whether or not the claimed compositions could be prepared, but whether they would provide an immune response capable of preventing or treating

HIV infection. As set forth *supra*, HIV vaccine development is characterized by unpredictability. The correlates of protection remain to be elucidated. Adequate animal modes that can be used to assess vaccine efficacy do not exist. Moroever, numerous clinical trials have resulted in failure. Applicants' response failed to provide any objective data addressing the numerous concers raised above. Accordingly the rejection is proper and hereby maintained.

Finality of Office Action

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications

may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

12 November, 2004